DEPARTMENT OF HEALTH & HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION

PHILADELPHIA DISTRICT
9 | 787a

900 U.S. Customhouse
2nd and Chestnut Streets
Philadelphia, PA 19106

Telephone: 215-597-4390

WARNING LETTER

CERTIFIED MAIL
RETURN RECEIPT REQUESTED

[redacted]

September 17, 2001

Mr. Willem de Goede
Executive Vice President & Chief Operating Officer
B. Braun Medical, Inc.
901 Marcon Boulevard
Allentown, PA 18109

Dear Mr. de Goede:

The Food and Drug Administration (FDA) has completed its review of the results of an inspection conducted at your medical device manufacturing facility located at 901 Marcon Boulevard, Allentown, Pennsylvania. The inspection was conducted between July 10 and 26, 2001, by Philadelphia District Investigators Michael J. Nerz and Kristen D. Evans. At the conclusion of the inspection, the investigators issued FDA form 483, Inspectional Observations, to C. Edward Brock, Vice President and General Manager, PA/NJ Operations, and discussed those observations with him and other individuals at your facility. A copy of this form is enclosed for your information.

Among other things, the inspection covered the manufacturing and ethylene oxide (EtO) sterilization of disposable IV administration sets. These products are devices within the meaning of Section 201(h) of the Federal Food, Drug, and Cosmetic Act (the Act). The inspection revealed serious deficiencies from the Quality System Regulation (QSR), which sets forth current Good Manufacturing Practice (cGMP) requirements for medical devices at Title 21 Code of Federal Regulations (21 CFR) Part 820. As a result, these products, and other devices manufactured at your facility are adulterated within the meaning of Section 501(h) of the Act, as described below:

> Failure to adequately validate processes which cannot be fully verified by subsequent inspection and test, 21 CFR 820.75, for example, the [redacted] process [redacted] used to manufacture disposable IV administration sets. Further, nonconforming disposable IV set extensions, rejected during processing on the [redacted]

[redacted] are not evaluated to determine the need for an investigation and/or impact on the manufacturing process. 21 CFR 820.90.

Failure to validate computer software used to (1) control the EtO sterilization process, for example, [redacted] cycles, and (2) control the [redacted]) employed in the manufacture of disposable IV sets, to ensure the software will perform for its intended use. 21 CFR 820.70(i).

Other deficiencies found during the inspection include failure to follow procedures for the cleaning and maintenance of manufacturing equipment, and failure to report Medical Device Regulation (MDR) reportable events in a timely manner.

At the conclusion of the inspection, firm officials promised to make corrections to the items listed in the FDA form 483, and reported that some of the observations had already been corrected. We acknowledge receipt of your letter dated September 4, 2001, and your representations concerning corrective actions. However, our preliminary review indicates that significant issues remain unresolved to our satisfaction. For example, you state that a comprehensive process validation was conducted on the [redacted] as a result of the inspection, but no documentation was provided to verify the adequacy of this corrective action. You indicated the [redacted] is out of service, however your response does not address the future operational status of this machine. This is of particular concern since it has not been validated.

Further, your response indicates you plan no further action with respect to disposable IV sets with leaking drip chambers in the marketplace based upon your conclusion, arrived at during the inspection, that the product presents 'little to negligible risk to the potential user'. We note, however, your own evaluation indicates that the 'probability of contamination depends on the size of the leak, the length of time the sterile system is open to contamination, and the cleanliness of the environment outside of the drip chamber' (undated Lomax email). Our review of your complaint records did not reveal any information concerning the size of the leak and the length of time the sterile system was open to contamination. The Lomax email postulates that it is unlikely a leak would escape the notice of a conscientious nurse for a significant period of time. If you have additional information on real use conditions impacting the size of leak and length of time, please provide this information in your response to this letter. You are advised FDA is reviewing this matter and will make its own assessment of the potential hazard to users.

This letter is not intended to be an all-inclusive list of deficiencies at your facility. As top management, it is your responsibility to assure that all of your company's operations are in compliance with the Act and its applicable regulations. The specific violations noted in this letter and in the FDA form 483 issued at the conclusion of the inspection may be symptomatic of serious

underlying problems in your establishment's quality system. You are responsible for investigating and determining the causes of the violations identified by the FDA. You also must promptly initiate permanent corrective and preventive action on your quality system.

You should take prompt action to correct these deviations. Failure to promptly correct these deviations may result in regulatory action being initiated by the FDA without further notice. These actions include, but are not limited to, seizure, injunction, and/or civil penalties.

We request you respond to this Warning Letter within 15 days, with documentation of corrections to violations identified in this letter, and in FDA form 483, Inspectional Observations, so an adequate assessment of your corrective actions can be completed by the Agency.

Your reply should be sent to the attention of Richard C. Cherry, Compliance Officer, at the address noted on the letterhead.

Sincerely,

Thomas D. Gardine

Thomas D. Gardine
District Director
Philadelphia District

Cc: Caroll H. Neubauer, CEO
B. Braun Medical, Inc.
824 Twelfth Avenue
Bethlehem, PA 18018

C. Edward Brock, Vice President & General Manager
B. Braun Medical, Inc.
901 Marcon Boulevard
Allentown, PA 18109

Kikoo Tejwani
Corporate Vice President Quality/Regulatory Compliance
B. Braun Medical, Inc.
2525 McGaw Avenue
P.O. Box 19791
Irvine, CA 92614-5895

Pennsylvania State Department of Health
132 Kline Plaza, Suite A
Harrisburg, PA 17104
Attention: Robert E. Bastian, Director
Division of Primary Care and
Home Health Services